

Applicants : Michael Wayne Graham and Robert Norman Rice  
Serial No. : 10/759,841  
Filed : January 15, 2004  
Page 2 of 73 of September 24, 2009 Amendment

**Amendments to the Claims** begin on page **3** of this document.

**Remarks** begin on page **12** of this document.

- Discussion of **Support for New Claims** begins on page **12**.
- A **Summary of February 12, 2009 Examiner Interview** begins on page **14**.
- Discussion of **Obviousness Rejections**:
  - **based on Fire et al. taken with Cowsert et al.** begins on page **15**;
  - **based on Agrawal et al. in view of Kool and Cowsert et al.** begins on page **48**.

**A Supplemental Information Disclosure Statement** begins on page **58** of this document.

Please amend the subject application as follows:

Applicants : Michael Wayne Graham and Robert Norman Rice  
Serial No. : 10/759,841  
Filed : January 15, 2004  
Page 3 of 73 of September 24, 2009 Amendment

### **Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-171. (Canceled)

172. (Currently Amended) A double-stranded ~~synthetic gene~~DNA construct comprising:

- a first structural gene sequence comprising 20-30 consecutive nucleotides identical in sequence to a region of a target gene encoding a viral DNA polymerase, a viral RNA polymerase or a viral coat protein in a mammalian cell;

- a second structural gene sequence comprising 20-30 consecutive nucleotides identical in sequence to, and in an inverted orientation relative to, the 20-30 consecutive nucleotides of the first structural gene sequence, such that a repeating sequence ~~of~~ which is only 20-30 consecutive nucleotides in length identical to the region of the target gene is present in the ~~synthetic gene~~DNA construct;

- a stuffer fragment which consists of nucleotides and which ~~is between~~ separates and links the first and second structural gene sequences;

- a promoter operable in the mammalian cell; and

- a transcription termination sequence active in the mammalian cell,

- wherein the repeating sequence within the ~~synthetic gene~~DNA construct is only 20-30 nucleotides in length, and

- wherein the first structural gene sequence, the stuffer fragment and the second structural gene sequence are all

Applicants : Michael Wayne Graham and Robert Norman Rice  
Serial No. : 10/759,841  
Filed : January 15, 2004  
Page 4 of 73 of September 24, 2009 Amendment

operably connected to the promoter and the transcription termination sequence.

173-175. (Canceled)

176. (Currently Amended) The double-stranded ~~synthetic-gene~~DNA construct of claim 172, wherein the region of the target gene is in an exon.

177. (Currently Amended) The double-stranded ~~synthetic-gene~~DNA construct of claim 172, wherein the target gene is from a lentivirus.

178. (Currently Amended) The double-stranded ~~synthetic-gene~~DNA construct of claim 172, wherein the target gene is from an immunodeficiency virus.

179. (Currently Amended) The double-stranded ~~synthetic-gene~~DNA construct of claim 172, wherein the target gene is from a single-stranded (+) RNA virus.

180. (Currently Amended) The double-stranded ~~synthetic-gene~~DNA construct of claim 172, wherein the target gene is a transgene in the mammalian cell.

181. (Currently Amended) The double-stranded ~~synthetic-gene~~DNA construct of claim 172, wherein the stuffer fragment is a sequence of nucleotides 10-50 nucleotides in length.

Applicants : Michael Wayne Graham and Robert Norman Rice  
Serial No. : 10/759,841  
Filed : January 15, 2004  
Page 5 of 73 of September 24, 2009 Amendment

182. (Currently Amended) The double-stranded ~~synthetic-gene~~DNA construct of claim 172, wherein the stuffer fragment is a sequence of nucleotides 50-100 nucleotides in length.
183. (Currently Amended) The double-stranded ~~synthetic-gene~~DNA construct of claim 172, wherein the stuffer fragment is a sequence of nucleotides 100-500 nucleotides in length.
184. (Currently Amended) The double-stranded ~~synthetic-gene~~DNA construct of claim 172, wherein the total length of the double-stranded ~~synthetic-gene~~DNA construct is no more than 0.5-2.0 kilobases.
185. (Currently Amended) The double-stranded ~~synthetic-gene~~DNA construct of claim 172, wherein the double-stranded ~~synthetic-gene~~DNA construct is in a virus particle.
186. (Currently Amended) The double-stranded ~~synthetic-gene~~DNA construct of claim 172, wherein the double-stranded ~~synthetic-gene~~DNA construct is in a liposome.
187. (Currently Amended) The double-stranded ~~synthetic-gene~~DNA construct of claim 172, wherein the double-stranded ~~synthetic-gene~~DNA construct is integrated into the genome of the mammalian cell.

Applicants : Michael Wayne Graham and Robert Norman Rice  
Serial No. : 10/759,841  
Filed : January 15, 2004  
Page 6 of 73 of September 24, 2009 Amendment

188. (Currently Amended) A mammalian cell having a ~~synthetic gene~~DNA construct comprising:

a first structural gene sequence comprising 20-30 consecutive nucleotides identical in sequence to a region of a target gene encoding a viral DNA polymerase, a viral RNA polymerase or a viral coat protein in the mammalian cell;

a second structural gene sequence comprising 20-30 consecutive nucleotides identical in sequence to, and in an inverted orientation relative to, the 20-30 consecutive nucleotides of the first structural gene sequence, such that a repeating sequence ~~of which is only~~ 20-30 consecutive nucleotides in length identical to the region of the target gene is present in the ~~synthetic gene~~DNA construct;

a stuffer fragment which consists of nucleotides and which is between and links the first and second structural gene sequences;

a promoter operable in the mammalian cell; and

a transcription termination sequence active in the mammalian cell,

wherein the repeating sequence within the ~~synthetic gene~~DNA construct is only 20-30 nucleotides in length, and

wherein the first structural gene sequence, the stuffer fragment and the second structural gene sequence are all operably connected to the promoter and the transcription termination sequence.

189. (Canceled)

Applicants : Michael Wayne Graham and Robert Norman Rice  
Serial No. : 10/759,841  
Filed : January 15, 2004  
Page 7 of 73 of September 24, 2009 Amendment

190. (Previously Presented) The mammalian cell of claim 188, wherein the region of the target gene is in an exon.
191. (Previously Presented) The mammalian cell of claim 188, wherein the target gene is from a lentivirus.
192. (Previously Presented) The mammalian cell of claim 188, wherein the target gene is from an immunodeficiency virus.
193. (Previously Presented) The mammalian cell of claim 188, wherein the target gene is from a single-stranded (+) RNA virus.
194. (Previously Presented) The mammalian cell of claim 188, wherein the target gene is a transgene in the mammalian cell.
195. (Previously Presented) The mammalian cell of claim 188, wherein the stuffer fragment is a sequence of nucleotides 10-50 nucleotides in length.
196. (Previously Presented) The mammalian cell of claim 188, wherein the stuffer fragment is a sequence of nucleotides 50-100 nucleotides in length.
197. (Previously Presented) The mammalian cell of claim 188, wherein the stuffer fragment is a sequence of nucleotides 100-500 nucleotides in length.
198. (Canceled)

Applicants : Michael Wayne Graham and Robert Norman Rice  
Serial No. : 10/759,841  
Filed : January 15, 2004  
Page 8 of 73 of September 24, 2009 Amendment

199. (Currently Amended) The mammalian cell of claim 188, wherein the ~~synthetic gene~~DNA construct is integrated into the genome of the mammalian cell.

200. (Currently Amended) An isolated mammalian cell, tissue or organ, having a ~~synthetic gene~~DNA construct comprising:

- a first structural gene sequence comprising 20-30 consecutive nucleotides identical in sequence to a region of a target gene encoding a viral DNA polymerase, a viral RNA polymerase or a viral coat protein in the mammalian cell;

- a second structural gene sequence comprising identical in sequence to, and in an inverted orientation relative to, the 20-30 consecutive nucleotides of the first structural gene sequence, such that a repeating sequence ~~of which is~~ only 20-30 consecutive nucleotides in length identical to the region of the target gene is present in the ~~synthetic gene~~DNA construct;

- a stuffer fragment which consists of nucleotides and which is between and links the first and second structural gene sequences;

- a promoter operable in the mammalian cell; and

- a transcription termination sequence active in the mammalian cell,

- wherein the repeating sequence within the ~~synthetic gene~~DNA construct is only 20-30 nucleotides in length, and

- wherein the first structural gene sequence, the stuffer fragment and the second structural gene sequence are all operably connected to the promoter and the transcription termination sequence.

201. (Canceled)

Applicants : Michael Wayne Graham and Robert Norman Rice  
Serial No. : 10/759,841  
Filed : January 15, 2004  
Page 9 of 73 of September 24, 2009 Amendment

202. (Previously Presented) The isolated mammalian cell, tissue or organ of claim 200, wherein the region of the target gene is in an exon.
203. (Previously Presented) The isolated mammalian cell, tissue or organ of claim 200, wherein the target gene is from a lentivirus.
204. (Previously Presented) The isolated mammalian cell, tissue or organ of claim 200, wherein the target gene is from an immunodeficiency virus.
205. (Previously Presented) The isolated mammalian cell, tissue or organ of claim 200, wherein the target gene is from a single-stranded (+) RNA virus.
206. (Previously Presented) The isolated mammalian cell, tissue or organ of claim 200, wherein the target gene is a transgene in the mammalian cell.
207. (Previously Presented) The isolated mammalian cell, tissue or organ of claim 200, wherein the stuffer fragment is a sequence of nucleotides 10-50 nucleotides in length.
208. (Previously Presented) The isolated mammalian cell, tissue or organ of claim 200, wherein the stuffer fragment is a sequence of nucleotides 50-100 nucleotides in length.



Applicants : Michael Wayne Graham and Robert Norman Rice  
Serial No. : 10/759,841  
Filed : January 15, 2004  
Page 10 of 73 of September 24, 2009 Amendment

209. (Previously Presented) The isolated mammalian cell, tissue or organ of claim 200, wherein the stuffer fragment is a sequence of nucleotides 100-500 nucleotides in length.
210. (Canceled)
211. (Currently Amended) The isolated mammalian cell, tissue or organ of claim 200, wherein the ~~synthetic gene~~DNA construct is integrated into the genome of the isolated mammalian cell, tissue or organ.
212. (New) The double-stranded DNA construct of claim 172, wherein the first structural gene sequence consists of 20 consecutive nucleotides identical in sequence to a region of a target gene encoding a viral DNA polymerase, a viral RNA polymerase or a viral coat protein in a mammalian cell, and the second structural gene sequence consists of 20 consecutive nucleotides identical in sequence to, and in an inverted orientation relative to, the 20 consecutive nucleotides in length identical to the region of the target gene.
213. (New) The mammalian cell of claim 188, wherein the first structural gene sequence consists of 20 consecutive nucleotides identical in sequence to a region of a target gene encoding a viral DNA polymerase, a viral RNA polymerase or a viral coat protein in a mammalian cell, and the second structural gene sequence consists of 20 consecutive nucleotides identical in sequence to, and in an inverted orientation relative to, the 20 consecutive nucleotides in length identical to the region of the target gene.

Applicants : Michael Wayne Graham and Robert Norman Rice  
Serial No. : 10/759,841  
Filed : January 15, 2004  
Page 11 of 73 of September 24, 2009 Amendment

214. (New) The isolated mammalian cell, tissue or organ of claim 200, wherein the first structural gene sequence consists of 20 consecutive nucleotides identical in sequence to a region of a target gene encoding a viral DNA polymerase, a viral RNA polymerase or a viral coat protein in a mammalian cell, and the second structural gene sequence consists of 20 consecutive nucleotides identical in sequence to, and in an inverted orientation relative to, the 20 consecutive nucleotides in length identical to the region of the target gene.